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Introduction

Exposures to cotton, hemp, and flax dust have been associated with two acute pulmonary responses: irritant (industrial) bronchitis and chest tightness (byssinosis). These symptoms, often accompanied by reduction in lung function, have occurred in 2 to 30 percent of cotton textile workers within hours of resuming exposure following a weekend or holiday (Schilling 1956; Morgan et al. 1982). These elements of the acute cotton dust pulmonary response may not occur together, and may represent responses of distinct pulmonary mechanisms. The exposure variables or host characteristics that lead to cough rather than to bronchoconstriction are currently under careful study (Hogg and Eggleston 1984). The effects of cigarette smoking upon these different responses is also incompletely understood.

In the manufacture of cotton textiles, cotton dust exposure occurs most intensely when the tightly packed bale is opened and when abrasive crushing and carding remove the "trash" (plant bracts and other parts, dirt, bacteria, and fungi) and align the fibers for spinning (Gideon and Johnson 1978). Normally, as the cotton fibers are spun, twisted, and woven into cloth, progressively less dust is generated. By the time cotton cloth is processed, the procedure is practically free of cotton dust (Kilburn 1983).

Cross-sectional studies have shown that byssinosis prevalence is greatest among cotton textile workers in the dusty preparation jobs (e.g., carder, stripper, or grinder) (Figure 1). Byssinosis prevalence has been related to the duration of cotton dust exposure, to the quality of the raw cotton, and to the levels of lint-free cotton dust (Molyneux and Tombleson 1970; Merchant, Lumsden, Kilburn, O'Fallon et al. 1973b; Kamat et al. 1981). At a cotton dust level of 0.2 mg/m^3 (lint-free dust of approximately 15 μm or less), approximately 15 percent of the cotton textile workers have some grade of byssinosis (Merchant, Lumsden, Kilburn, O'Fallon et al. 1973b). While a small sex-specific effect (male disadvantage) has been noted (Berry et al. 1974), no age effect has been shown after adjustment for exposure (Merchant, Lumsden, Kilburn, O'Fallon et al. 1973b; Berry et al. 1974). Cigarette smoke interacts with cotton dust exposure in cotton textile workers and has been associated with increased byssinosis prevalence and severity (Berry et al. 1974). The frequency of byssinosis has been closely correlated with the presence of chronic bronchitis, and both symptoms have been associated with ventilatory impairment (Imbus and Suh 1973). Cross-sectional studies have correlated cotton dust exposure with two components of ventilatory impairment: reduction in the baseline level of forced expiration and reversible loss of function across a work shift. The relationship of byssinosis and bronchitis with ventilatory impairment and its

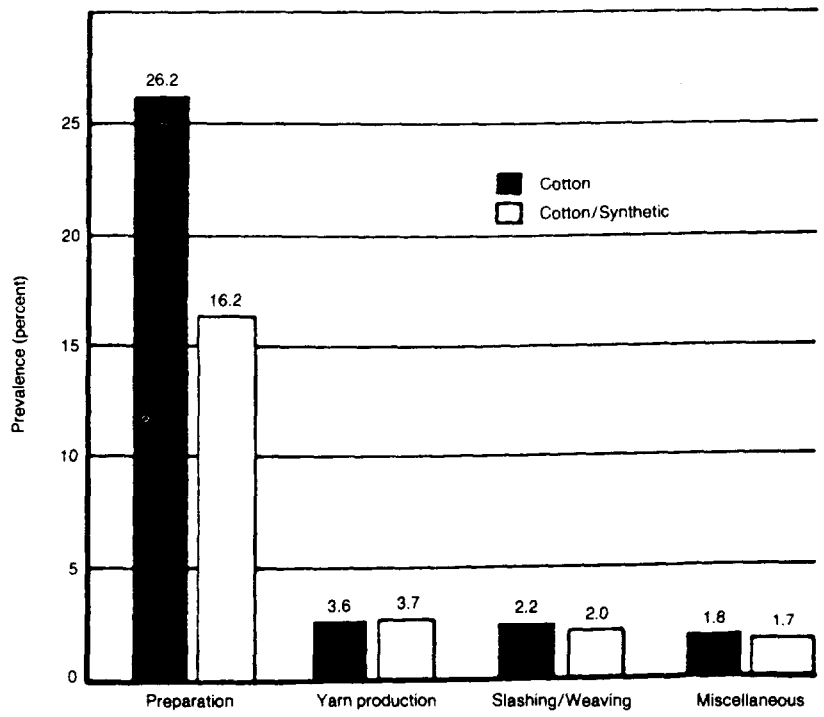


FIGURE 1.—Byssinosis prevalence by work area and raw material use

NOTE: Average prevalence: cotton, 5.2 percent; cotton/synthetic, 4.4 percent.
SOURCE: Imbus and Suh (1973).

relationship to cigarette smoking is discussed in greater detail later in this chapter.

Influence of Cigarette Smoking on the Natural History of Byssinosis

Cigarette Smoking Patterns Among Workers Exposed to Cotton Dust

The smoking patterns of cotton dust exposed workers have been reported by a number of authors and are presented in Table 1.

In summary, current studies show that male cotton workers tend to smoke to a greater degree than do female cotton workers. Male textile workers in Western Europe and in Canada smoke with

TABLE 1.—Prevalence of smoking in studies of cotton workers

Study	Number and type of population	Smoking characteristics (percent)				Comments
Schrag and Gullett (1970)	509 cotton textile workers		SM 38	EX/NS		Percent smoking <1 pack/day not available
Kari-Koskinen and Hirvonen (1970)	987 female cotton workers, Finland	Age	16.9	83.1		>53% began smoking at 15–19 years of age
		17–29	39.8			
		30–39	14.1			
		40–49	9.0			
		50–60	5.0			
Merchant, Kilburn, et al. (1972)	435 cotton-synthetic blend workers, North Carolina		SM 54.7	EX 12.0	NS 33.3	
Kilburn, Kilburn et al. (1973)	1,046 female textile workers, North Carolina		SM			
		Syn. wool workers	45.2			
		Cottonmill workers	35.8			
Szymczykiewicz et al. (1970)	637 men, 2,530 women	Men	80.5			
		Women	8.9			
Fox et al. (1973)	Cotton workers, 35 mills, Great Britain		SM 62	NS 31.6	EX 6.3	
		Cigs/day				
		1–14	38.2			
		15–24	21			
		>24	2.8			

TABLE 1.—Continued

Study	Number and type of population		Smoking characteristics (percent)		Comments
Imbus and Suh (1973)	10,133 cotton workers, North Carolina		Men Women	78 43	Smokers include ever smoked 1 cig/day for 1 year
Berry et al. (1974)	14 cotton and 2 manmade fiber mills, Great Britain		Men Women	75.6 56.5	Former smokers not reported
Zuskin et al. (1976)	Wool workers and controls	Workers	Men Women	47 0	
		Controls	Men Women	55 0	
Khogali (1976)	271 ginnery workers, Sudan			SM 36.5	Almost 1/2 smokers said smoked <5 cigs/day
Jones et al. (1977)	153 cottonmill workers, southeast United States			SM/EX 70	
Bouhuys et al. (1977)	Card and weave room workers, South Carolina			SM	
			Men Women	18–41 15–25	

TABLE 1.—Continued

Study	Number and type of population	Smoking characteristics (percent)				Comments
Palmer et al. (1978)	203 gin workers		SM	EX	NS	*( )=mean pack-years (1 pk/day/year)
		Ginners	51.1 (16.0)*	25.5 (9.6)	23.4	
		Pressmen	57.1 (7.3)	19.1 (4.1)	23.8	
		Others	45.5 (15.3)	15.1 (8.0)	39.4	
		Controls	52.3 (11.4)	19.2 (9.1)	28.5	
Bouhuys et al. (1979)	Textile workers, aged ≥45, South Carolina	Women	SM	EX	NS	
		Carding	18	14	68	
		Spinning	20	10	70	
		Preparing	17	14	69	
		Weaving	20	10	69	
		Others*	15	11	74	*Includes cloth room workers and miscellaneous job categories
		Men				
		Carding	26	44	26	
		Spinning	37	45	18	
		Preparing	50	42	8	
		Weaving	38	37	18	
		Others*	20	35	30	
Jones et al. (1979)	Cotton and wool/synthetic mill workers		SM*	NS		*Smokers include ex-smokers
		Mill 1	52.8	47.2		
		Mill 2	66.9	33.1		
		Mill 3	64.8	35.2		
		Mill 4	38.0	62.0		

TABLE 1.—Continued

Study	Number and type of population	Smoking characteristics (percent)			Comments
			SM	EX	
Barman (1979)	70 cottonmill workers	Men	44	28	
		Women	58		
Sparks and Peters (1980)	Cotton dust-exposed workers	Men	44	28	
		Women	55	—	
Grimard and Adams (1981)	Textile workers, Canada	Men	76.6		
		Women	60.4		
Beck et al. (1982)	118 male and 162 female cotton textile workers	Men			
		Workers	27		
		Controls	16		
		Women			
		Workers	31		
		Controls	43		

NOTE: SM = Smoker; EX = Ex-smoker; NS = Nonsmoker.

greater frequency than do American workers, with many studies showing the proportion of smokers to be well over 70 percent.

Acute Effects of Smoking and Cotton Dust Exposure on Respiratory Symptoms

The symptoms of Monday chest tightness begin gradually, 3 or 4 hours after the cotton textile worker returns to work. A dry cough and shortness of breath on exertion frequently accompany the sensation of chest tightness. However, the physiologic reaction associated with Monday chest tightness is not confined to the chest. A low grade temperature, a 20 to 30 percent increase in the peripheral white blood cell (polymorphonuclear leukocyte) count, and a general malaise have been frequently reported. These systemic symptoms suggest the presence of a host inflammatory response; however, the relationship between these systemic symptoms and the symptom of chest tightness is not well defined.

By 1936, an association had been recognized between Monday chest tightness and detectable loss of ventilatory capacity and increased breathlessness (Prausnitz 1936). Recognition that in susceptible cotton mill workers, Monday chest tightness may be followed by permanent respiratory disability led to the evolution of a standard byssinosis case definition. Schilling and colleagues (1955) developed specific questions concerning Monday chest tightness for the British Medical Research Council's respiratory symptom survey questionnaire (*British Medical Journal* 1960). A positive response to the standardized questions regarding Monday chest tightness defined the presence of byssinosis.

Molyneux and Tombleson (1970) conducted one of the first prospective studies of byssinosis. At the initial examination, these investigators interviewed 1,359 workers from 14 cotton spinning mills and 227 workers from 2 manmade fiber spinning mills in Lancashire, United Kingdom. Followup examinations were conducted at 6-month intervals over 3 years, from 1963 to 1966. Byssinosis and bronchitis prevalence were determined by the use of the Medical Research Council's questionnaire on respiratory symptoms (*British Medical Journal* 1960), to which the Roach and Schilling (1960) questions on chest tightness were added. Byssinosis was graded as follows (Molyneux and Tombleson 1970):[1]

Grade 0: No evidence of chest tightness or breathing difficulty on the first day of the workweek

Grade 1/2: Occasional chest tightness on Mondays

[1] Note: Other investigators have used grade [illegible] to indicate the presence of chronic obstructive pulmonary disease (COPD). Rooney et al. 1969. However, this category would also include the chronic obstructive pulmonary disease that occurs secondary to cigarette smoking among cotton workers since COPD occurs frequently [illegible] is not specific for disease related to cotton dust exposure.

Grade 1: Chest tightness or difficulty in breathing on Mondays only

Grade 2: Chest tightness or difficulty in breathing on Monday and other days

Age, length of exposure to cotton dust, and smoking habit were determined by questionnaire. Individuals were considered smokers if they regularly smoked one or more cigarettes per day. Hexlet and total dust air samplers were used to measure the mass concentration of the respirable, medium, and fly components of the total airborne dust.

Byssinosis prevalence (adjusted for age, sex, and mill type) showed a progressive increase with increasing duration of cotton dust exposure (Table 2) (Molyneux and Tombleson 1970). A rearrangement of the data from this Lancashire mill workers study and calculation of the Mantel-Haenszel (weighted) odds ratios (Mantel 1963) shows an interesting relationship between smoking, byssinosis, bronchitis, and sex. A similar relationship is demonstrated by data from studies of American cotton mill workers (Merchant et al. 1972; Imbus and Suh 1973). Cigarette smoking was associated with an overall 2.21-fold excess risk of bronchitis in the Lancashire cotton mill workers (Table 3). Cotton mill workers of both sexes who smoked had a consistently greater prevalence of bronchitis than did nonsmokers. The magnitude of the smoking effect was similar for men (2.28-fold) and women (2.16-fold). The presence of bronchitis conferred an approximately twofold excess risk of developing byssinosis (Table 4). This risk was significant for men and for women, for smokers as well as for nonsmokers. Once the presence of bronchitis had been controlled for, however (Table 5), cigarette smoking did not add significant additional risk for developing byssinosis.

One may interpret these observations to show that among cotton mill workers both cotton dust exposure and cigarette smoking produced the symptoms of bronchitis. Bronchitis, in turn, seemed to confer additional risk for the development of acute chest tightness (byssinosis). Cigarette smoking, therefore, seems to facilitate the development of byssinosis in smokers exposed to cotton dust, perhaps by the prior induction of bronchitis. Applying an additive logit model (6 dust levels x 3 lengths of exposure x 4 combinations of sex and smoking habit) to these data, Berry and colleagues (1974) found that cigarette smokers had a modest (1.4-fold) increase in the adjusted prevalence of byssinosis when compared with nonsmokers and ex-smokers. Two years after the initial questionnaire survey, these investigators were able to reinterview about half of the original population (669 cotton workers and 127 manmade fiber workers). Incidence and remission rates were tabulated for byssinosis and bronchitis by length of exposure, sex, and smoking status. The incidence of both bronchitis and byssinosis was greater among

TABLE 2.—Prevalence (percent) of byssinosis in nine exposure groups

Exposure (yr)	Number in group	Observed prevalence	Prevalence adjusted for age	Prevalence adjusted for age, mill type, and sex
0–4	305	5.2	8.8	8.0
5–9	155	23.3	20.5	19.2
10–14	168	28.0	22.3	21.0
15–19	187	35.8	29.5	27.5
20–24	117	36.8	30.9	31.1
25–29	115	43.5	40.2	42.4
30–34	94	30.9	30.2	35.1
35–39	99	35.4	36.5	41.4
≥40	119	33.6	37.7	41.8

SOURCE: Molyneux and Tombleson (1970).

TABLE 3.—Age-adjusted association of bronchitis and smoking, by byssinosis status and sex

	Bronchitis with byssinosis			Bronchitis without byssinosis			Chi square and odds ratio for the association of smoking/bronchitis[1]
Smoker	N	Present	Absent	N	Present	Absent	
				Men			
Yes	127	55%	45%	301	46%	54%	$X^2=15.20$
No	33	55%	45%	105	21%	79%	OR=2.28 ($p<0.0001$)
				Women			
Yes	125	48%	52%	322	31%	69%	$X^2=21.10$
No	78	33%	67%	268	16%	84%	OR=2.16 ($p<0.0001$)
Chi Square[2]:		$X^2=2.83$			$X^2=36.8$		
Odds Ratio[2]:		OR=1.49 ($p=0.09$)			OR=2.63 ($p<0.0001$)		
Chi Square[3]:							$X^2=36.3$
Odds Ratio[3]:							OR=2.21 ($p<0.0001$)

[1] Weighted by Mantel-Haenszel technique for byssinosis frequency.
[2] Weighted by Mantel-Haenszel technique for sex distribution.
[3] Weighted by Mantel-Haenszel technique for frequency of both byssinosis and sex.
SOURCE: Molyneux and Tombleson (1970).

smokers than among nonsmokers or ex-smokers of both sexes; however, these differences were not statistically significant (Berry et al. 1974).

TABLE 4.—Age-adjusted association of bronchitis and byssinosis by smoking status and sex

Association of byssinosis and bronchitis	Odds ratio	p-Value
Men and women combined		
Cigarette smoker	1.73	0.0002
Nonsmoker	3.13	<0.0001
Combined smoking status		
Men	1.80	0.001
Women	2.25	<0.0001
Combined overall	2.02	<0.0001

SOURCE: Data from Molyneux and Tombleson (1970).

TABLE 5.—Age-adjusted association of byssinosis and smoking by bronchitis status and sex

Association of byssinosis and smoking	Odds ratio	p-Value
Men and women combined		
Bronchitis present	0.82	0.39
Bronchitis absent	1.44	0.03
Combined bronchitis status		
Men	1.19	0.45
Women	1.17	0.36
Combined overall	1.18	0.23

SOURCE: Data from Molyneux and Tombleson (1970).

More than 10,000 Burlington Industries textile employees (95 percent of the workforce) from 19 plants participated in a 1970 survey conducted by Duke University with the cooperation of Burlington Industries and the North Carolina State Board of Health (Imbus and Suh 1973). Each participant received the modified British Medical Research Council Respiratory Questionnaire for determining the prevalence of byssinosis and bronchitis. Byssinosis was graded according to the classification of Roach and Schilling (1960). Chronic bronchitis was defined as grade 0, no evidence of sputum production; grade 1, simple chronic bronchitis; and grade 2, chronic bronchitis with an exacerbation (Imbus and Suh 1973). Smokers were defined as those regularly smoking one or more cigarettes per day (Molyneux and Tombleson 1970). Forced expiration was measured in all participants before the beginning of the work shift on the first day of the workweek. Approximately 80

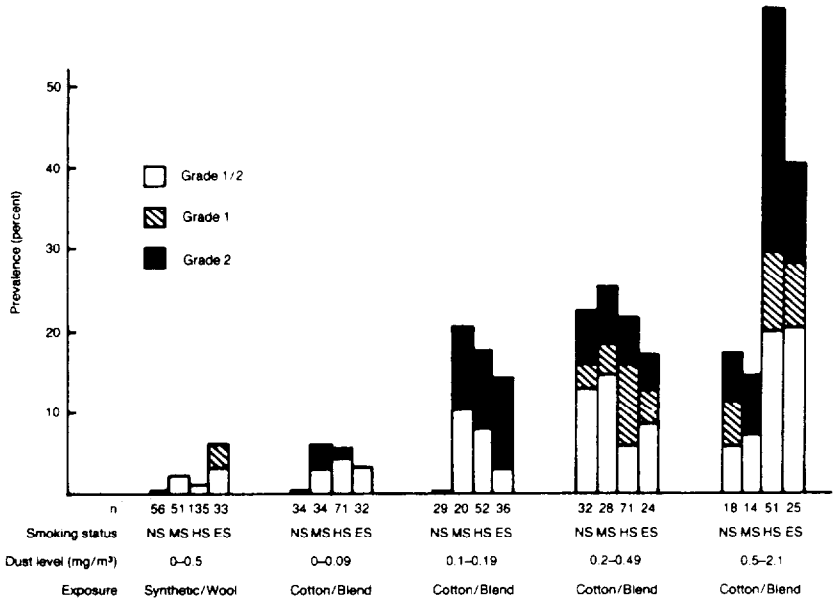


FIGURE 2.—Byssinosis prevalence by grade, smoking status, and dust level among men working in synthetic/wool mills and cotton/blend mills, North Carolina, 1970–1971

SOURCE: Merchant, Lumsden, Kilburn, O'Fallon et al. (1973a)

percent underwent spirometry again 6 hours into the work shift (Imbus and Suh 1973).

Like Molyneux and Tombleson (1970) in their study of the Lancashire mill workers, the North Carolina investigators found that smoking was responsible for a doubling of the bronchitis risk and that the presence of bronchitis was strongly associated with byssinosis. After controlling for the effect of bronchitis, there was no additional significant smoking effect on the risk of chest tightness at the observed dust levels. Cigarette smoking seemed to play a greater role in byssinosis prevalence as cotton dust levels rose (smoking–cotton dust interaction). Figure 2 shows no cigarette smoking effect on byssinosis prevalence at low dust levels. However, at the highest dust levels, cigarette smoking was found to interact with cotton dust exposure to substantially increase the acute symptom prevalence (Merchant et al. 1972; Merchant, Lumsden, Kilburn, O'Fallon et al. 1973a).

No "safe" level of cotton dust exposure has been identified for cigarette smokers (Merchant, Lumsden, Kilburn, O'Fallon et al. 1973b). However, among nonsmokers, these investigators found no case of byssinosis below a cotton dust level of 0.2 mg/m^3. An

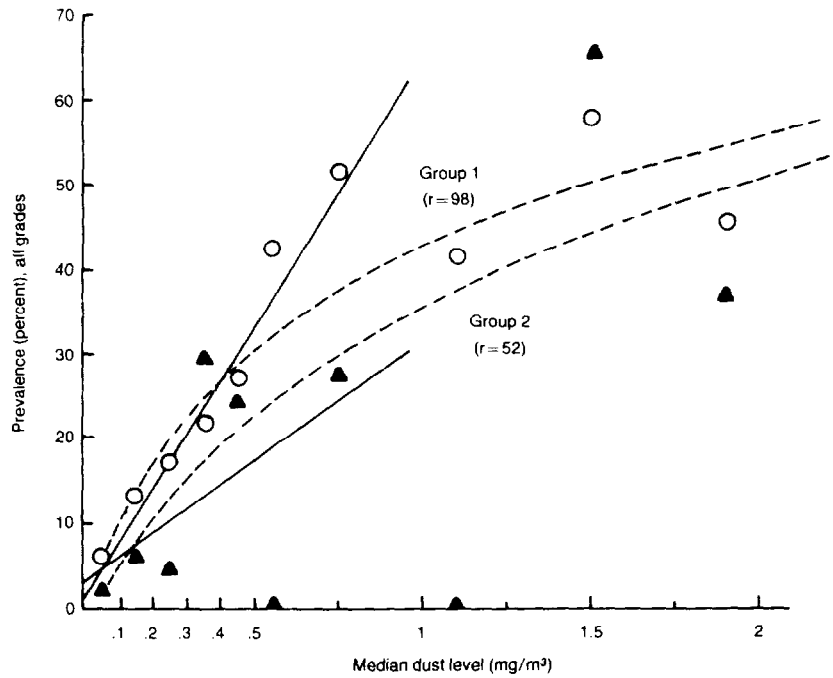


FIGURE 3.—Byssinosis prevalence by median dust level among current smokers and those who never smoked, preparation and yarn area workers, linear regressions and fitted profit dose–response curves

NOTE: Group 1 (○), smokers; group 2 (△), nonsmokers.
SOURCE: Merchant, Lumsden, Kilburn, O'Fallon et al. (1973b).

examination of a large population found one case in a nonsmoker below this level (Figure 3). Workers with byssinosis who stopped smoking but did not change their work area lost their byssinosis symptoms (Merchant et al. 1972). These observations suggest that there may be a "safe" level of cotton dust in the absence of other inhaled irritants. Cigarette smoking seems to lower this threshold of susceptibility to chest tightness below the present limits of cotton dust detection. At least in some individuals, this threshold may be restored by smoking cessation.

The repeated demonstration of a linear dose–response relationship of symptoms with cotton dust levels led to the development of cotton dust exposure standards to protect the majority of the workforce (Roach and Schilling 1960; McKerrow et al. 1962; Merchant et al. 1972; Merchant, Lumsden, Kilburn, O'Fallon et al. 1973b). The

American Congress of Government Industrial Hygienists' (ACGIH) early cotton dust standard was based upon the work of Roach and Schilling (1960), which concluded that 1 mg/m^3 gross (total) dust was a safe level for occupational exposure. Further study, however, found that the biologic activity of cotton dust resided primarily in the respirable dust fraction (McKerrow et al. 1962). The use of total dust as the only measure of exposure has sometimes resulted in a misleading lack of association between cotton dust level and byssinosis symptoms (McKerrow et al. 1962; Molyneux and Tombleson 1970; Merchant et al. 1972).

High correlations between byssinosis symptoms and respirable dust levels were observed, using the vertical elutriator to sample dust of an aerodynamic diameter of 15 μm and less (Merchant, Lumsden, Kilburn, O'Fallon et al. 1973b). In Figure 3, cigarette smokers are shown to have a slightly higher prevalence of byssinosis symptoms than nonsmokers at each measured dust level. A linear dose–response model fits the data at low dust levels. At respirable dust levels from 0.1 to 0.75 mg/m^3, the byssinosis prevalence in nonsmokers rose from 5 to 24 percent, and in smokers, from 8 to 53 percent. The tapering of the dose–response curve at higher dust levels has been attributed to self-selection by less susceptible cotton workers (Kilburn 1983).

To minimize the acute symptoms and to inhibit possible chronic consequences, the Occupational Safety and Health Administration (OSHA) (US DOL 1981) has modified the permissible exposure limits to acknowledge the importance of the respirable fraction of cotton dust (approximately 15 μm or less aerodynamic equivalent diameter). The OSHA standard specifies that employees engaged in yarn manufacturing may not be exposed to respirable cotton dust levels greater than 0.200 mg/m^3 over an 8-hour average, and employees assigned to the slashing/weaving processes can be exposed to no more than an 8-hour average of 0.750 mg/m^3 of cotton dust (US DOL 1981). No specific accommodation has been made to recognize the increased byssinosis susceptibility of cigarette smokers.

Effects of Smoking and Cotton Dust Exposure on Pulmonary Function Tests

In a cross-sectional study of 61 textile workers on carding machines, Zuskin and colleagues (1975) found a rough correlation between the grade of byssinosis and the 1-second forced expiratory volume (FEV_1) before dust exposure. These observations confirm those of Merchant, Halprin and colleagues (1974) (Figure 4). It is suggested that those with byssinosis symptoms start the workweek with a lower FEV_1 than those without symptoms (age, height, sex, race unaccounted for), and at least for the individuals with byssinosis grade 1/2, that overnight exposure cessation is insufficient for

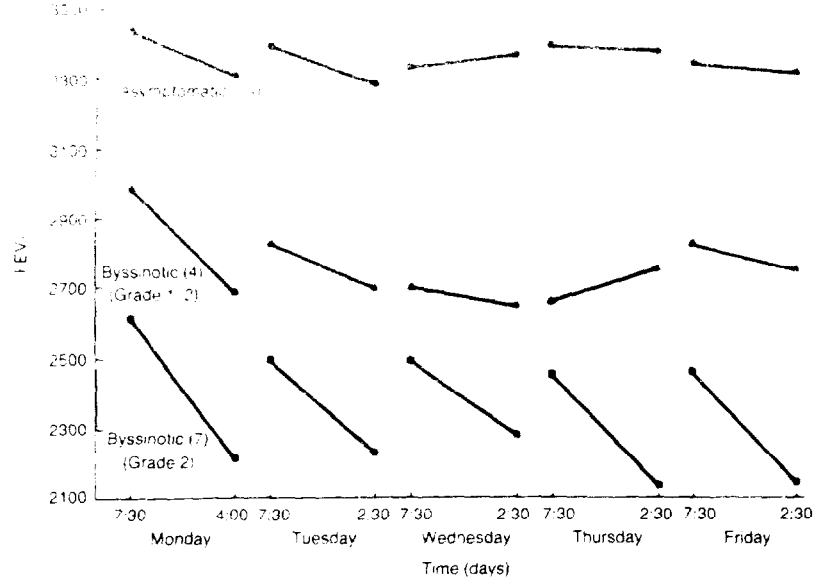


FIGURE 4.—FEV_1 during 5-day exposure of 25 carders
SOURCE: Merchant, Halprin et al. (1974).

complete respiratory recovery and that a longer abstinence period (a weekend, for example) is necessary to restore preexposure levels of ventilatory function (Merchant, Halprin et al. 1974).

The baseline (initial) ventilatory function, measured as percent of predicted FEV_1 and forced vital capacity (FVC), showed that among nonsmokers (Table 6), a mild decrease was noted in those with bronchitis alone (without byssinosis) and a more marked decrease was observed in those with byssinosis alone (without bronchitis). In men, the lowest value was observed among bronchitics with byssinosis. Smoking further reduced the baseline ventilatory function in every category (except nonbronchitic, byssinotic women). (The authors pointed out that the small sample size may have made the slightly higher ventilatory function value among this group of women somewhat uncertain.) There was also an interaction of the effects of cigarette smoking with cotton dust exposure upon baseline forced expiration, similar to that found for symptoms of chest tightness (Merchant, Lumsden, Kilburn, O'Fallon et al. 1973b).

Studies of pulmonary function among 61 textile workers showed that cotton dust exerts its acute effect primarily upon the conducting airways rather than upon the gas-exchanging parenchyma (Zuskin et al. 1975). Zuskin and colleagues observed a significant reduction

TABLE 6.—Average percentage of predicted FEV_1 in smokers and nonsmokers with and without byssinosis and bronchitis

Subjects	Average percent of predicted FEV_1 (sample size)	
	Nonbyssinotic	Byssinotic
Male nonsmokers		
Nonbronchitic	89.4 (993)	84.5 (28)
Bronchitic	88.2 (59)	80.1 (16)
Male smokers		
Nonbronchitic	85.9 (3,172)	81.5 (157)
Bronchitic	81.2 (434)	73.7 (109)
Female nonsmokers		
Nonbronchitic	85.7 (1,729)	76.6 (47)
Bronchitic	82.9 (68)	78.4 (11)
Female smokers		
Nonbronchitic	82.6 (1,213)	77.0 (30)
Bronchitic	81.3 (93)	73.5 (15)

SOURCE: Imbus and Suh (1973).

across a workshift in FEV_1 and midexpiratory flow at 50 percent ($MEF_{50\%}$) and a statistically significant increase in residual volume. In contrast, plethysmographically determined total lung capacity (a measure of alveolar volume) and the single-breath diffusing capacity (a measure of gas diffusion) were unchanged.

In Figures 5 and 6 are shown the effects of byssinosis, bronchitis, and smoking on FEV_1 measured before and after 6 hours' work, adjusted to a base age of 40 years. People with bronchitis alone (without byssinosis) and people with byssinosis alone (without bronchitis) experience a decline in FEV_1 during the workday. People with a combination of both conditions, however, show the greatest decrement. Although forced expiration change across a work shift also shows a strong association with dust levels (Merchant, Lumsden, Kilburn, O'Fallon et al. 1973b), the relationship of cigarette smoking to the cross-shift decline in function is less clear. Merchant, Lumsden, Kilburn, O'Fallon, and colleagues (1973a) found no smoking effect on acute ventilatory function change within any dust level, over all dust levels, or as part of a dust times smoking interaction (Merchant, Lumsden, Kilburn, O'Fallon et al. 1973a). Zuskin and colleagues (1969) and Jones and colleagues (1979) reported similar observations. However, Haglind and Rylander

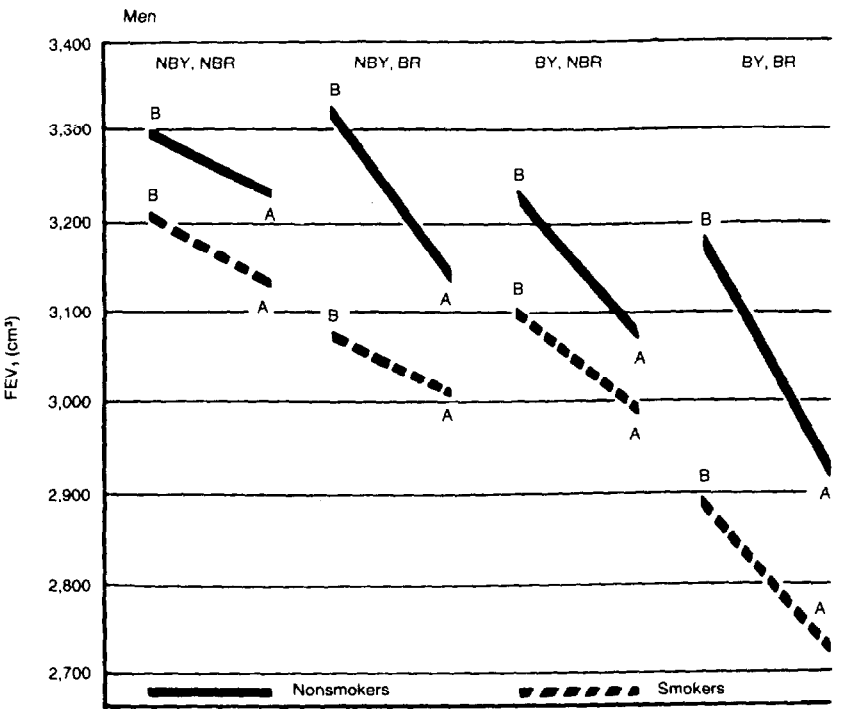


FIGURE 5.—Byssinosis, bronchitis, and smoking effects on FEV_1 in men before and after 6 hours' work, adjusted to base age 40 years

NOTE: B, before work; A, after 6 hours' work.
SOURCE: Imbus and Suh (1973).

(1984) found that cigarette smokers seemed to have a lower effect threshold. Among cigarette smokers, the threshold for a 5 percent decrease in FEV_1 was 0.58 mg dust/m^3, compared with a threshold in nonsmokers nearly threefold greater (1.63 mg/m^3). These results confirmed the findings of Merchant and colleagues (1975) among a group of 12 cotton workers in an exposure chamber. In addition to the lower threshold, Haglind and Rylander (1984) reported a larger FEV_1 decrease among smokers than among nonsmokers at the same exposure levels. These findings and the others previously mentioned suggest that cigarette smoke may enhance the airways reaction to cotton dust.

Cross-shift change in ventilatory function has been shown to depend upon the type of cotton dust as well as the level (Table 7)

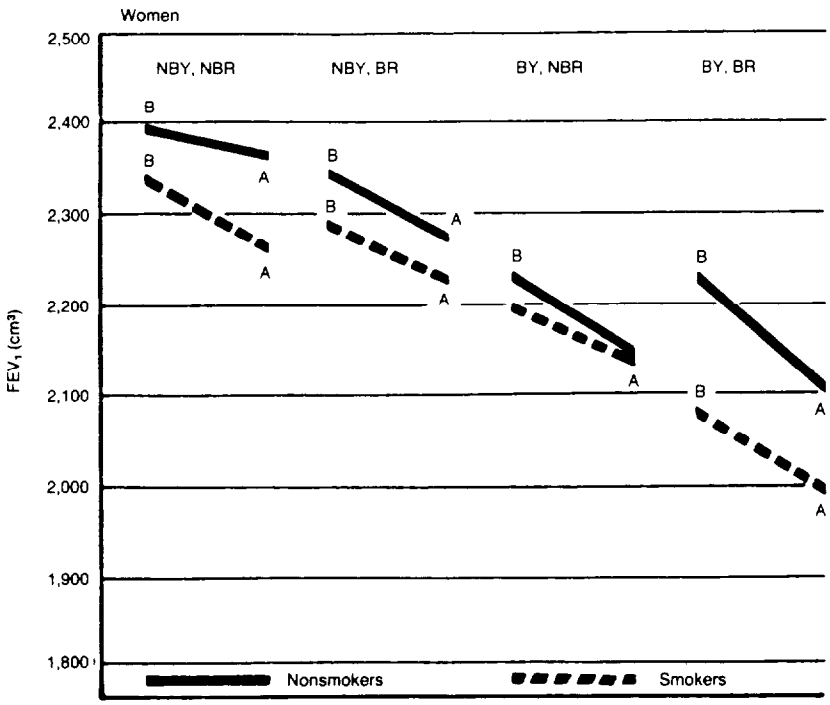


FIGURE 6.—Byssinosis, bronchitis, and smoking effects on FEV_1 in women before and after 6 hours' work, adjusted to base age 40 years

NOTE: B, before work; A, after 6 hours' work.
SOURCE: Imbus and Suh (1973).

(Schilling 1956; Roach and Schilling 1960; Merchant, Lumsden, Kilburn, O'Fallon et al. 1973b; Merchant et al. 1975; Castellan et al. 1984). Under the conditions of an experimental card room (using carding machines under typical commercial production conditions), concentrations of gravimetric elutriated cotton dust and the corresponding acute FEV_1 change were measured (Table 7). In Figure 7 is shown the significant association of dust concentration and ventilatory response found by Castellan and colleagues (1984). Bacterial endotoxin, a contaminate of cotton dust, was found in this study to correlate even more closely with a decline in ventilatory function, but Diem and colleagues (1984) found that the across-shift decline was more closely correlated with the log dust level than with the number of gram negative rods or log endotoxin level.

TABLE 7.—Slopes of dose–response regressions for individual cottons, using vertically elutriated gravimetric dust as an exposure index

Cotton type	Change (percentage per mg/m³ of dust)		
	FVC	FEV_1	$FEF_{75\%}$
California strict middling	-0.9[1]	-0.4[1]	+4.0[1]
California strict low middling	-2.3[2]	-3.4[3]	-18.0[3]
California strict low middling spotted	-2.7[3]	-3.1[3]	-13.2[2]
Texas strict low middling	-2.3[3]	-2.9[3]	-18.4[3]
Texas strict low middling spotted	-3.6[3]	-6.2[3]	-27.3[3]
Mississippi strict low middling	-3.1[3]	-3.5[3]	-20.1[3]
Mississippi strict low middling spotted	-15.9[3]	-24.4[3]	-88.6[3]

NOTE: Regressions based on spirometric responses of 54 persons. FVC = forced vital capacity; FEV_1 = forced expiratory volume in 1 second; $FEF_{75\%}$ = maximal flow at 75 percent of expired vital capacity.

[1] p = not significant

[2] $p < 0.01$.

[3] $p < 0.0001$.

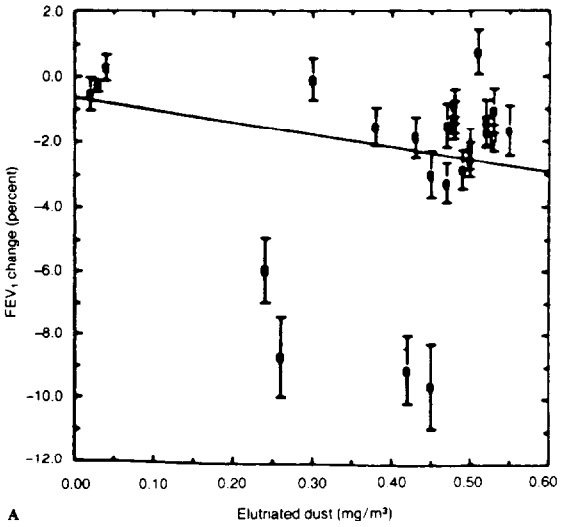
SOURCE: Castellan et al. (1984).

Chronic Clinical Effects of Cotton Dust Exposure

Nonreversible reduction in forced expiration is usually caused by an increase in airways resistance (particularly in the small airways), a reduction in elastic recoil (emphysema), or both (Bates et al. 1971). Chronic cough and sputum production may be a nonspecific irritant reaction to particle deposition in the conducting airways. Similar reactions have been seen in cigarette smokers and workers exposed in dusty trades including mining (coal and metal), manufacturing (cement and plastics), and foundry work (Morgan and Seaton 1975; Hankinson et al. 1977; Morgan 1978; Kilburn 1983).

Chronic airflow obstruction is associated with increased age-adjusted total mortality and respiratory disease mortality. However, once adjustment has been made for airflow obstruction, cough and chronic mucus hypersecretion (the symptoms of chronic bronchitis) have little additional predictive value for chronic obstructive lung disease (COLD) mortality (Peto et al. 1983). Since there are both significant morbidity and mortality consequences associated with the development of chronic obstruction but not with simple bronchitis, it is important to determine whether the acute symptoms of bronchitis and chest tightness associated with cotton dust exposure are associated with chronic airflow obstruction to a greater extent than could be explained by cigarette smoking alone.

The contribution of the acute byssinotic symptoms (grades 1/2 and 1) to the subsequent development of airflow obstruction and the chronic forms (grades 2 and 3) of byssinosis is not well documented (Douglas et al. 1984). The term "byssinosis" is often applied to the acute response to inhalation of cotton dust as well as to the



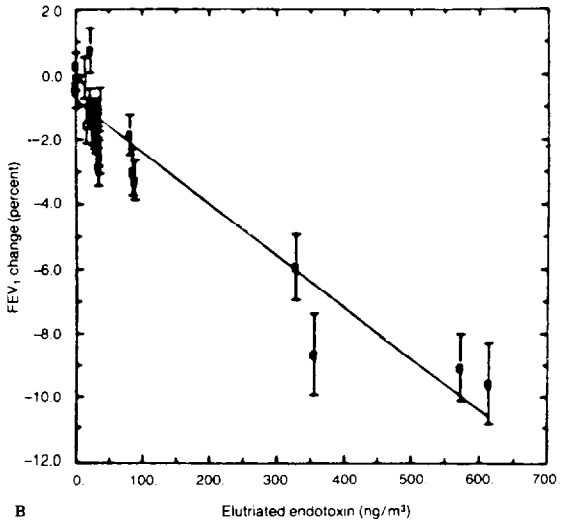


FIGURE 7.—Percentage of change in forced expiratory volume in 1 second (FEV_1) (mean±SE) for each subgroup of people exposed for 6 hours to a clean room and to dust from various cottons (54 persons in two equal-sized subgroups; seven different cottons)

NOTE: A. Plot of change in FEV_1 (percent) versus vertically elutriated airborne gravimetric dust concentration (mg/m^3); B. Plot of change in FEV_1 (percent) versus vertically elutriated airborne endotoxin concentration (ng/m^3).
SOURCE: Castellan et al. (1984).

permanent dyspnea with impaired function. Although a link of pathogenesis between the two has been assumed, and is supported by finding impairment in textile workers without other exposures, no longitudinal study has been done that documents this transition (Kilburn 1983).

Nevertheless, chronic airflow obstruction has been found more frequently in cotton textile workers than in control populations (Bouhuys et al. 1977; Wegman et al. 1983). Obstruction has been found particularly among the older, cigarette-smoking cotton textile workers (Merchant, Lumsden, Kilburn, O'Fallon et al. 1973a; Beck, Maunder, and Schachter 1984). Whether cotton textile workers are compared with a control population of synthetic fiber and wool workers (Merchant, Lumsden, Kilburn, O'Fallon et al. 1973a), with farmers and workers from other industries (Bouhuys et al. 1969), or with the population of a rural town (Beck, Schachter, and Maunder 1984), there is a cross-sectional correlation between occupational exposure to cotton dust and impaired ventilatory function.

Followup studies that document a greater fall in ventilatory function among those with byssinosis help to establish the transition between acute and chronic effect (Bouhuys and Zuskin 1976). Beck, Schachter, and Maunder (1984) have compared the frequency of pulmonary function abnormality among South Carolina cotton textile workers with the pulmonary function survey results among residents of a Connecticut community. These researchers report that both byssinosis and smoking were associated with subsequent impairment of age- and height-adjusted respiratory function. They found that even asymptomatic cotton textile workers had significant lung function impairment compared with controls. In general, cotton textile workers had lower lung function among smokers and nonsmokers, for both men and women and among those with and without symptoms, but these differences were only statistically significant for the nonsmoking asymptomatic female subgroup (the subgroup with the largest number of individuals). Smokers also had lower FEV_1 than nonsmokers in each of the subgroups. However, in the absence of cotton dust measurements, nonoccupational factors related to control selection may be postulated to have contributed to these findings (Tockman and Baser 1984).

Other followup studies of cotton textile workers provide inconsistent support for the importance of byssinosis to subsequent ventilatory impairment. Zuskin and Valic (1975) reported on a 10-year followup of selected members of a worker cohort exposed to coarse cotton dust. These investigators found both an increased prevalence of byssinosis on followup examination and approximately twice the rate of mean annual decline in FEV_1 among men who had byssinosis initially, compared with those who later developed it or to those who did not report this symptom. Smoking was not found to contribute

significantly to the development of byssinosis. Contrasting results were reported by Berry and colleagues (1973), who examined cotton textile workers at several plants and found that the cotton textile workers had a 54 mL per year decline in FEV_1 compared with 32 mL per year in workers in the synthetic textile mill; however, most of this excess decline could be attributed to workers in only one mill. FEV_1 declined 19 mL per year faster in smokers than in nonsmokers. However, despite these differences between the cotton workers and the control group, no difference in annual FEV_1 decline was found between the subjects with and without byssinosis symptoms. Cotton textile workers with acute (grades 0 or 1) byssinosis symptoms and those with bronchitis following cotton dust exposure may be a subset of the population at risk of further ventilatory deterioration. The sensitivity and specificity of these symptoms for subsequent lung injury is yet to be established by cohort studies.

Followup studies of cotton textile workers have been weakened by several sources of bias. Self-selection of workers for continued employment in dusty environments introduces bias into studies that examine only the currently available workforce, who may be healthier than workers who have left the industry. Berry and colleagues (1973) reported that less than half of the subjects were available sufficiently often to calculate an annual FEV decline. Merchant, Lumsden, Kilburn, O'Fallon, and colleagues (1973b) reported substantial evidence of selection away from dust exposure in the cotton textile industry, which results in the presence of relatively resistant workers in dustier areas at the time of cross-sectional surveys. As Beck, Schachter, and Maunder (1984) have shown, it is feasible to survey the retired workforce in addition to those currently active in order to account for workers who retire prematurely because of poor respiratory health. To finally determine the magnitude of the cotton dust effect on chronic lung function of cotton textile workers, studies must carefully distinguish the separate indices of cotton dust lung injury, and impairment rates must be tabulated over the entire population at risk. However, documentation of the association between exposure and lung injury will become increasingly difficult as industrial hygiene control reduces the levels of occupational cotton dust exposure.

Mechanisms of Cotton Dust Lung Injury

Epidemiologic observations have suggested that cigarette smoking and cotton dust have complementary effects on the airways. A discussion of the mechanisms of cotton dust lung injury may facilitate an understanding of this interaction.

Inflammation (Bronchitis)

Considerable effort has been devoted to the search for specific agents responsible for the symptoms and changes in lung function associated with cotton dust exposure. These investigations have focused upon water-soluble extracts found in the cotton bract. An animal model has been developed that partly reflects the sequence of clinical findings seen in cotton textile workers. Hamster inhalation of condensed vegetable tannins from card room floor sweepings stimulated the recruitment of leukocytes to the trachea, bronchi, and small bronchioles, with a time course similar to that of byssinosis symptoms in humans (Kilburn, Lynn et al. 1973). Tannins isolated from cotton bract have been shown to cause pneumocyte lysis (Ayars et al. 1984). Other agents in cotton dust have also been found to have pharmacologic activity (Hitchcock 1974; Ainsworth et al. 1979). Compounds that have been identified in cotton bract extract in significant concentrations include tannin, 5-hydroxytryptamine, endotoxin, and histamine (Rylander 1981; Bouhuys and Lindell 1961; Rohrbach et al. 1984; Russell et al. 1982).

Pharmacologic activity has also been isolated from the components of bacteria and fungi found in cotton bract. Studies by Cinkotai and colleagues (1977) have demonstrated a close relationship between the prevalence of byssinotic symptoms and the airborne concentration of gram-negative (endoagar) bacteria. In Figure 8 are shown a close correlation between byssinotic symptoms and levels of gram-negative bacteria, a more variable relationship with gram-positive (nutrient agar) bacteria, and no relationship with fungi or with airborne dust. Human exposure to airborne gram-negative bacteria may result in symptoms related to the presence of endotoxin lipopolysaccharide within the bacterial cell walls (Rylander 1982). This material could activate complement (Wilson et al. 1980) with subsequent generation of anaphylatoxins, release of histamine and leukotactic substances, and induction of an inflammatory response.

Cotton bales from different geographic areas may be contaminated with different levels of gram-negative bacteria. Cottons grown in dry areas with irrigation were found to have smaller amounts of gram-negative bacteria (Rylander et al. 1985). The culturing of viable organisms was found to be a misleading index of byssinosis potency, however, because endotoxin activity persists after bacterial death (Rylander et al. 1985). Airborne endotoxin levels correlated with byssinosis symptoms, blood neutrophil levels, and airways response (Rylander et al. 1985). Castellan and colleagues (1984) have reported a high correlation between endotoxin exposure and ventilatory fall in experimental exposures (part B of Figure 7). Their data show no evidence for an endotoxin exposure threshold, but this conclusion depends on the validity of the four outlying observations presented in the figure. In an experimental card room, Haglind and Rylander

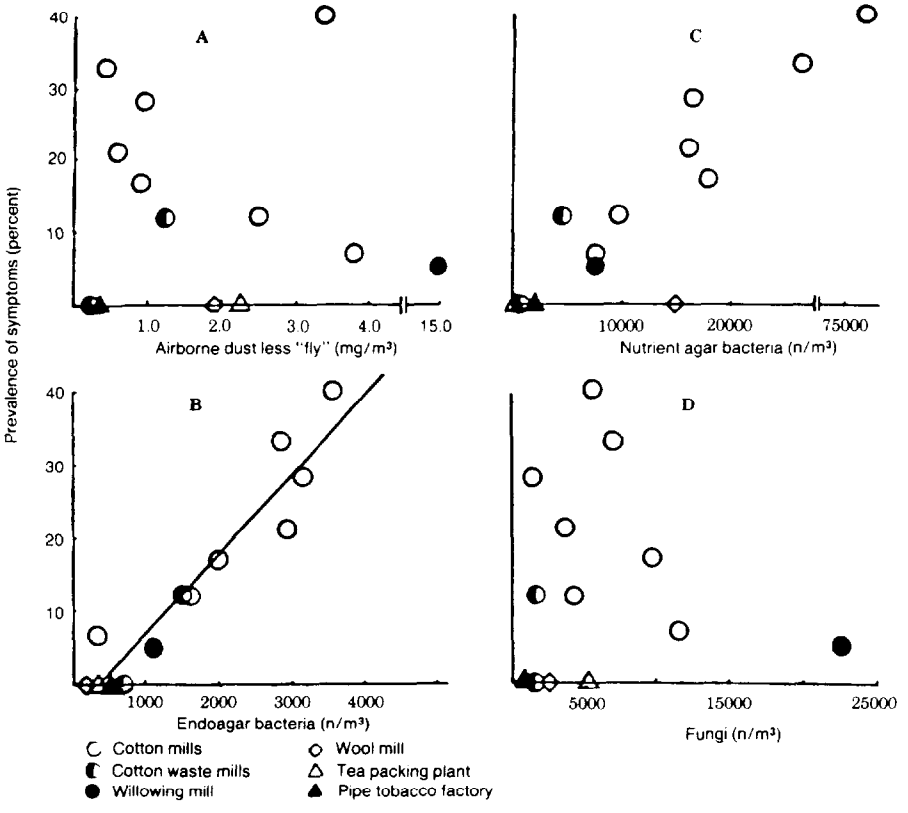


FIGURE 8.—Concentration of endotoxins in airborne dust correlated with the prevalence of byssinotic symptoms

SOURCE: Cinkotai et al. (1977).

(1984) found a dose–response relationship between the average FEV_1 decrement across a work shift and the amount of airborne dust or endotoxin. These data have been used to suggest that endotoxin contamination of cotton, rather than the plant dust itself, is responsible for the byssinosis syndrome. However, Buck and colleagues (1984) have reported that cotton bract extract contains a bronchoconstricting agent or agents distinct from endotoxin and have suggested that an interaction may exist between the effects of endotoxin and these other agents; Diem and colleagues (1984) have